



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Linda M. Pacioretti *et al.*

Application No.: 10/699,195

Filing Date: 10/31/2003

Docket Number: CLANACCR_001NP

Title: **COMPOSITIONS AND METHODS FOR THE
TREATMENT OF HIV-ASSOCIATED FAT
MALDISTRIBUTION AND HYPERLIPIDEMIA**

Examiner: Chong, Young Soo

Art Unit: 1617

CERTIFICATE OF TRANSMISSION

I hereby certify that this correspondence is being deposited with the United States Postal Service as "EXPRESS MAIL" MAILING LABEL NUMBER EO 942 516 565 US in an envelope addressed to MAIL STOP RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date indicated below.

Date: 12/24/07



John G. Babisch

MAIL STOP RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
Sir:

DECLARATION PURSUANT TO 37 C.F.R. § 1.132

I, John G. Babisch declare as follows:

- 1) I am Dr. John G. Babisch, Chairman, Bionexus, Ltd. I have held this position since June 1997.

2) I have Doctorate and Masters degrees, respectively, in Biochemistry and Chemistry from Cornell University, as well as a Bachelor degree in Biochemistry from The Pennsylvania State University. A copy of my Curriculum Vitae is attached as Exhibit A.

3) I am also an inventor named in 50 domestic patent applications including U.S. Application Nos. 10/699,195; 10/141,085; 10/789,814; 10/789,817; 10/988,393; 10/480,145; 10/484,123; 10/881,404; 10/774,048; 10/464,834; 10/234,002 and 09/952,632 and 16 issued domestic patents, including U.S. Patent Nos. 7,279,185; 7,270,835; 6,733,793; 6,140,063; 5,506,420; 6,629,835; 6,733,793 and 6,908,630.

4) On the basis of 30 years of training and experience, I am an expert in the art of molecular biology of pharmaceuticals and xenobiotics. I was a faculty member at the College of Veterinary Medicine, Cornell University for 17 years. As Professor of Pharmacology and Toxicology, my research program involved the elucidation of mechanisms by which xenobiotics affect signaling pathways in normal and transformed cells. Using the tools of molecular biology such as monoclonal antibodies, northern and western blotting and enzyme-linked immunoassays, my research program developed cell-based assays for the identification of small molecules directed at inhibiting selected cellular functions. Findings from these studies were used to identify potential anti-viral and anti-neoplastic pharmacophores from natural products. My research has also identified both positive and negative drug-drug and drug-nutrient interactions.

5) Additionally, I have served as Senior Pharmacologist in two clinical studies involving the testing of dietary supplements in HIV-positive subjects. In one of these studies the objective was to assess the effects of the supplement formulation on lipodystrophy (fat maldistribution) in HIV-positive subjects receiving highly active anti-retroviral treatment (HAART). During the two-year course of this study, I developed an understanding of the clinical presentation of lipodystrophy (fat maldistribution) associated with HIV infection.

5) I understand that in the course of the Office Action mailed April 13, 2007, Claims 1-20, 25-27, 30-31, 36-38 were withdrawn as a result of a restriction requirement.

Additionally, Examiner Young Soo Chong rejected Claim(s) 21 (in part), 22-24, 28-29, 32 (in part), 33-35, and 39-40 were rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over McCleary (US Patent Application 2002/0132219A1, hereinafter “McCleary”). As cited by the Examiner, McCleary teaches: ¶0002 Disorders of nutrient partition include obesity (fat maldistribution) and hyperlipidemia. The parenthetic term “fat maldistribution” does not appear in McCleary and appears to be a conclusion drawn by the Examiner. The term obesity is not defined in McCleary.

6) Among researchers in the field and those skilled in the art, Stedman’s Medical Dictionary is considered the reference standard for defining medical terms. Stedman’s Medical Dictionary [26th edition] defines obesity as, “An abnormal increase of fat in the subcutaneous connective tissues.” Note that in the context of this definition, the increased fat accumulation in obesity occurs in the subcutaneous tissue layer as opposed to only in the visceral location. This teaches away from the fat maldistribution seen in HIV-1 patients treated with HAART, as those persons loose subcutaneous fat as noted in the instant application (see ¶0010 and ¶0051) and the purpose of the invention is to increase subcutaneous fat (see ¶0024, 0025 and 0035).

7) Conclusion. Stedman’s Medical Dictionary [26th edition] defines obesity as, “An abnormal increase of fat in the subcutaneous connective tissues.” This teaches away from the fat maldistribution seen in HIV-1 patients treated with anti-retroviral therapy, as those persons loose subcutaneous fat.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 12/24/07



John G. Babisch, Ph.D.
Chairman, Bionexus, Ltd.
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Ithaca, NY 14850

Exhibit A**BIOGRAPHICAL SKETCH AND BIBLIOGRAPHY**

John G. Babis

Chairperson, BIONexus, Ltd.

Executive Vice President, Metaproteomics Inc.

Education

<u>Institution and Location of Study</u>	<u>Degree</u>	<u>Date Conferred</u>	<u>Field</u>
The Pennsylvania State University, State College, PA	B.S.	1968	Biochemistry
Cornell University, Ithaca, NY	M.S.	1974	Chemistry
Cornell University, Ithaca, NY	Ph.D.	1976	Biochemistry

Research and Professional Experience

Aug. 2002 – present	Executive Vice President of Research & Development, Metaproteomics, Research Laboratories, Ithaca, NY. Metaproteomics develops clinically proven, patented dietary supplements and pharmaceuticals from natural sources. Duties include the design and evaluation of experiments elucidating mechanism of action and biological activity within complex mixtures.
1998 – present	(5% Effort) National Coordinator for the USDA Minor Species Drug Program (NRSP-7). The NRSP-7 program is funded by the USDA to provide funds and expertise necessary for the approval of pharmaceuticals used in the treatment of diseases associated with minor crop species. Duties include the coordination of industrial, academic and regulatory resources necessary for protocol development through final drug approval.
1997 – present	Co-founder and Chairperson of BIONexus, Ltd. Ithaca, NY. BIONexus develops and markets nutritional supplements to address health problems associated with AIDS. NutriVir™, the BIONexus supplement for wasting in HIV/AIDS, generated approximately \$600,000 in gross revenues in its first year of sales. NutriVir™ is reimbursed by Medicaid in 14 states.
1991 – 1996	Founder, Chairperson, President and CEO of Paracelsian, Inc., Ithaca, NY. The Company was launched from the technology transfer program of Cornell University in 1991, and with the public offering in 1992 (Nasdaq, PRLN), became the first public corporation of a Cornell University technology transfer effort. Babis was

associated with the attainment of over \$12 million dollars in corporate financing.

1984 – 1996	Tenured, Associate and Professor of Pharmacology and Toxicology, Department of Pharmacology, College of Veterinary Medicine, Cornell University. Offered the first course in molecular risk assessment in the USA in 1979; member of the graduate Fields of Pharmacology, Toxicology, Veterinary Medicine, Food Science and Epidemiology; successfully petitioned the State of New York for the approval of the separate Fields of Toxicology and Pharmacology at Cornell University.
1978 – 1984	Assistant Professor, Department of Preventive Medicine, NYS College of Veterinary Medicine, Cornell University, Ithaca, NY.
1976 – 1978	Postdoctoral Scientist, Food and Drug Research Labs, Waverly, NY.

Invited Presentations (Recent of 38 presentations)

Micronutrient deficiencies in AIDS wasting at Progressive Management of AIDS Wasting: 2000. Hunter College, NYC. March 24, 2000.

Phytochemicals and NF- κ B activation at IBC's Conference on The Health Benefits of Natural Phytoceuticals. Montreal Bonaventure Hilton, July 22 – 23, 1997.

Chemically-induced cell cycle stasis in immunotoxicology. 12th Annual NIOSH Conference on Mechanisms of Immunotoxicology – Role of Apoptosis in Immunotoxicology. University of West Virginia, Morgantown, WV. September 10 – 12, 1997.

Publications (Selected of 108 peer-reviewed publications)

Hall AJ, Tripp M, Howell T, Darland G, Bland JS, Babisch JG. (2006) Gastric mucosal cell model for estimating relative gastrointestinal toxicity of non-steroidal anti-inflammatory drugs. *Prostaglandins Leukot Essent Fatty Acids.* 75(1):9-17.

Payne M.A., Babisch J.G., Bulgin M., Lane M., Wetzlich S., Craigmill A.L. (2002) Serum pharmacokinetics and tissue and milk residues of oxytetracycline in goats following a single intramuscular injection of a long-acting preparation and milk residues following a single subcutaneous injection. *J Vet Pharmacol Ther.* 25(1):25-32.

Calabrese C., Berman S.H., Babisch J.G., et al. (2000) A phase I trial of andrographolide in HIV positive patients and normal volunteers. *Phytother Res.* 14(5):333-338.

Ma,X., Stoffregen,D.A., Wheelock,G.D., Rininger,J.A. and Babisch,J.G. (1997) Discordant hepatic expression of the cell division control enzyme p34cdc2 kinase, proliferating cell nuclear antigen, p53 tumor suppressor protein, and p21Waf1 cyclin-dependent kinase inhibitory protein after WY14,643 ([4-chloro-6-(2,3-xylylidino)-2-pyrimidinylthio]acetic acid) dosing to rats. *Mol. Pharmacol.*, 51, 69-78.

Rininger,J.A., Goldsworthy,T.L. and Babisch,J.G. (1997) Time course comparison of cell-cycle protein expression following partial hepatectomy and WY14,643-induced hepatic cell proliferation in F344 rats. *Carcinogenesis*, 18, 935-941.

Rininger,J.A., Stoffregen,D.A. and Babisch,J.G. (1997) Murine hepatic p53, RB, and CDK inhibitory protein expression following acute 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) exposure. *Chemosphere*, 34, 1557-1568.

Rininger,J.A., Wheelock,G.D., Ma,X. and Babisch,J.G. (1996) Discordant expression of the cyclin-dependent kinases and cyclins in rat liver following acute administration of the hepatocarcinogen [4-chloro-6-(2,3-xylidino)-2-pyrimidinylthio] acetic acid (WY14,643). *Biochem. Pharmacol.*, 52, 1749-1755.

Vancutsem,P.M. and Babisch,J.G. (1996) In vitro and in vivo study of the effects of enrofloxacin on hepatic cytochrome P-450. Potential for drug interactions. *Vet. Hum. Toxicol.*, 38, 254-259.

Patents (Selected of 16 US and three foreign patents)

US Patent No. 7,279,185	Curcuminoid compositions exhibiting synergistic inhibition of the expression and/or activity of cyclooxygenase-2.
US Patent No. 6,733,793	Oral composition with insulin-like activities and methods of use.
US Patent No. 5,833,994	Use of the Ah receptor and Ah receptor ligands to treat or prevent cytopathicity of viral infection.
US Patent No. 5,612,188	Automated, multicompartimental cell culture system.
US Patent No. 5,529,899	Immunoassay for Ah receptor transformed by dioxin-like compounds.
US Patent No. 5,496,703	Indirect immunoassay for dioxin-like compounds